Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Fluorouracil chemotherapy: the My5-FU assay for guiding dose adjustment.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Fluorouracil chemotherapy: the My5-FU assay for guiding dose adjustment. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Dec 10. 47 p. (Diagnostics guidance; no. 16).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The My5-FU assay is only recommended for use in research for guiding dose adjustment in people having fluorouracil chemotherapy by continuous infusion. The My5-FU assay shows promise and the development of robust evidence is recommended to demonstrate its utility in clinical practice.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Cancers treated with continuous intravenous infusion of 5-fluoruracil (5-FU) chemotherapy including:

- Colorectal cancer
- Head and neck cancer

- Stomach cancer
- Pancreatic cancer

Guideline Category

Evaluation

Technology Assessment

Clinical Specialty

Gastroenterology

Internal Medicine

Oncology

Otolaryngology

Pathology

Pharmacology

Intended Users

Advanced Practice Nurses

Clinical Laboratory Personnel

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To evaluate the clinical effectiveness and cost-effectiveness of the My5-FU assay for the pharmacokinetic dose adjustment of continuous infusion 5-fluorouracil (5-FU) chemotherapy

Target Population

Cancer patients receiving 5-fluorouracil (5-FU) by continuous venous infusion

Interventions and Practices Considered

Pharmacokinetic dose adjustment and therapeutic drug monitoring of 5-fluorouracil (5-FU) using the My5-FU assay

Major Outcomes Considered

- Accuracy of My5-FU assay (e.g., correlation between My5-FU and 'gold standard')
- Proportion of patients with 5-fluorouracil (5-FU) plasma levels in the optimal target range
- Area-under-the-curve (AUC) measurements
- Incidence of over- and under-dosing

- Frequency of dose adjustment
- Test failure rates
- Treatment response rates
- Progression-free survival
- Overall survival
- Incidence of 5-FU toxicity and side effects
- Quality of life
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an External Assessment Group to perform a systematic literature review on the technology considered in this diagnostics guidance and prepare a Diagnostics Assessment Report (DAR). The DAR for this evaluation was prepared by Warwick Evidence (see the "Availability of Companion Documents" field).

Clinical Effectiveness Methods

Identification and Selection of Studies

Search Strategies for Clinical Effectiveness

Scoping searches were undertaken to inform the development of the search strategies and to assess the volume and type of literature relating to the assessment questions. An iterative procedure was used, with input from clinical advisors and the NICE Diagnostics Assessment Programme manual. One search strategy was developed for Objectives A, B and C and another two were developed for Objective D (see Section 3.2 in the DAR for description of objectives A, B, C, D, and E). Search strategies are presented in Appendix 1 in the DAR.

Searches for Objectives A, B and C

This search strategy focussed on My5-FU/gold standard technologies, fluorouracil, pharmacokinetics and dose adjustment, with a limit to English language. No study type or date limits were applied. This search strategy developed for EMBASE was adapted as appropriate for other databases. The searches were undertaken in January 2014. All retrieved papers were screened for potential inclusion.

The search strategy comprised the following main elements:

- Searching of electronic bibliographic databases
- Contact with experts in the field
- Scrutiny of references of included studies
- Screening of manufacturer's and other relevant organisations' websites for relevant publications

Bibliographic databases:

MEDLINE; MEDLINE In-Process & Other Non-Indexed Citations; EMBASE; Cochrane Library (including Cochrane Systematic Reviews, Database of Abstracts of Reviews of Effectiveness [DARE], CENTRAL, National Health Service Economic Evaluation Database [NHS EED], and Health Economic Assessment [HTA] databases); Science Citation Index and Conference Proceedings (Web of Science); National Institute

for Health Research (NIHR) Health Technology Assessment Programme; PROSPERO (International Prospective Register of Systematic Reviews).

The following trial databases were also searched: Current Controlled Trials; ClinicalTrials.gov; UK Clinical Research Network (UKCRN) Portfolio Database; World Health Organisation (WHO) International Clinical Trials Registry Platform.

See Section 4.1.1.1 in the DAR (see the "Availability of Companion Documents" field) for other searches (specific conference proceedings and websites).

Searches for Objective D

Several UK guidelines and evidence updates based on systematic reviews were identified via searches or personal communication. Two search strategies were then developed focussing on finding systematic reviews on the use of fluorouracil in metastatic colorectal cancer (mCRC) and head and neck (H&N) cancer (see Appendix 1 in the DAR). H&N cancer was not considered further in Objective D. The searches were limited to English language and to articles published in or after 2011. A focussed search filter for systematic reviews developed in house was used. This search filter will miss less well-reported reviews (e.g., where the terms systematic or meta-analysis are not included in the title or abstract), but recent initiatives, such as Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), mean that this is less of a concern than in the past. The search strategies developed for Medline were adapted as appropriate for other databases. The searches were undertaken in April 2014.

Bibliographic databases:

MEDLINE; MEDLINE In-Process & Other Non-Indexed Citations; Cochrane Library (Cochrane Systematic Reviews, DARE and HTA databases).

The following website was consulted via the Internet:

Saladax http://www.saladax.com/

See Section 4.1.2 of the DAR for inclusion and exclusion of relevant studies for Objectives A to D.

Review Strategy

The general principles recommended in the PRISMA statement were used. Records rejected at full text stage and reasons for exclusion were documented. Two reviewers independently screened the titles and abstracts of all records identified by the searches and discrepancies were resolved through discussion. Disagreement was resolved by retrieval of the full publication and consensus agreement. Full copies of all studies deemed potentially relevant, were obtained and two reviewers independently assessed these for inclusion; any disagreements were resolved by consensus or discussion with a third reviewer.

Cost-effectiveness and Health Economics

Methods

Search Strategy

A comprehensive search of the literature for published economic evaluations, utility studies and cost studies was performed. Several search strategies were required. Searches were undertaken in March and April 2014. Additional searches were undertaken to identify other relevant information to support the development of the economic model (e.g., past NICE assessments in mCRC).

Cost Search 1: Cost Effectiveness of PK Dosing and 5-FU

The search strategy developed for objectives A, B and C (see Section 3.2 of the DAR for description of objectives A, B, C, and D) of the clinical effectiveness review (for methods, see "Search Strategies for Clinical Effectiveness" above and Appendix 2 in the DAR) was also used to identify any published cost-effectiveness studies. This was considered appropriate because no study type filters were applied. Full copies of all studies deemed potentially relevant by clinical effectiveness reviewers were obtained and assessed by a health economist for inclusion.

Cost Search 2: Adverse Events Associated with Chemotherapy (All Cancers): Quality of Life

A series of search strategies was devised to update and expand a previously published literature review. The search strategies were developed iteratively and are provided in Appendix 1 of the DAR. Searches were undertaken in Medline and EMBASE. All records were screened for inclusion by an information specialist and checked by a health economist. Full copies of all studies deemed potentially relevant were obtained and

assessed by a health economist for inclusion.

Cost Search 3: Adverse Events Associated with Chemotherapy (All Cancers): Resource Use

A scoping search was undertaken to look for existing reviews. Some reviews of interest were identified, but no relevant overarching review was found. Therefore, a search strategy was developed based on the strategies used for Cost search 2. The search strategies were developed iteratively and are provided in Appendix 1 in the DAR. Searches were undertaken in Medline. All records were screened for inclusion by an information specialist and checked by a health economist. Full copies of all studies deemed potentially relevant were obtained and assessed by a health economist for inclusion.

Cost Search 4: mCRC/H&N Cancer: Quality of Life and Cost Search 5: mCRC/H&N Cancer: Resource Use

Searches 4 and 5 were developed iteratively, with reference to the search strategies of several published systematic reviews. Searches for resource use were limited to English, Humans and the UK perspective (by the addition of several currency and location terms). No date limits were applied. Searches were undertaken in Medline (see Appendix 1 in the DAR). All records were screened for inclusion by an information specialist and checked by a health economist. Full copies of all studies deemed potentially relevant were obtained and assessed by a health economist for inclusion.

Inclusion Criteria for Studies to Address Objective E

All study designs will be considered for inclusion. Studies will be included that provide information on the following:

- Cost of My5-FU testing
- Cost of delivering 5-FU by infusion
- Cost of side effects and 5-FU toxicity and their associated treatment or hospitalisation costs
- Additional costs associated with changes to continuous infusion protocols

As no full text economic evaluation studies were identified, no studies were assessed using the Consolidation Health Economic Evaluation Reporting Standards (CHEERS) checklist.

Number of Source Documents

Clinical Effectiveness Results

Search Results for Objectives A, B and C

Figure 6 in the Diagnostics Assessment Report (DAR) (see the "Availability of Companion Documents" field) provides the PRISMA flow diagram for Objectives A, B and C. A total of 3,751 records were identified through electronic searches. One additional record was identified from other sources. The removal of duplicates left 2,565 records to be screened, of which 2,362 were excluded at title/abstract level as these were irrelevant. The remaining 203 records were examined for full-text, of which 35 were included in the clinical effectiveness review (see Appendix 7 in the DAR).

Search Results for Objective D

Figure 26 in the DAR provides the PRISMA flow diagram for Objective D. Electronic searches identified 67 records; an additional record was identified from other sources. After removal of 12 duplicates, 55 records were screened of which 50 were excluded as irrelevant at title/abstract level. Five records were examined at full text and one was included.

Full details on the reasons for excluding studies are full-text can be found in Appendix 8 in the DAR (see the "Availability of Companion Documents" field).

Cost-effectiveness and Health Economics

Results

Figure 35 in the DAR provides the PRISMA flow diagram for Objective E (cost-effectiveness). A total of 4,578 records were identified through electronic searches. Twelve additional records were identified from other sources. The removal of duplicates left 3,614 records to be screened, of which 3,514 were excluded at title/abstract level as these were irrelevant. The remaining 100 records were examined for full-text, of which 54 were included in the cost-effectiveness review.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an External Assessment Group to perform a systematic literature review on the technology considered in this diagnostics guidance and prepare a Diagnostics Assessment Report (DAR). The DAR for this evaluation was prepared by Warwick Evidence (see the "Availability of Companion Documents" field).

Clinical Effectiveness Methods

Identification and Selection of Studies

Data Extraction Strategy

Data were extracted by one reviewer, using a piloted, data extraction form (see Appendices 2 to 4 in the DAR). A second reviewer checked the extracted data and any disagreements were resolved by consensus or discussion with a third reviewer.

Data Extraction for Objective A-1 (see Section 3.2 in the DAR for description of objectives A, B, C, D, and E)

A data extraction sheet (see Appendix 2 in the DAR) was developed combining basic study information, results, and fields from the data extraction sheets for the other objectives so these data can be linked. The key measure for whether My5-FU can be considered equivalent to liquid chromatography mass spectrometry/mass spectrometry (LC-MS/MS) and high performance liquid chromatography (HPLC) is whether both the upper and lower limits of agreement (mean difference ±2 standard deviations [sd]) on the Bland-Altman plot are sufficiently small that they can be considered clinically equivalent. Additionally, if the 95% confidence interval (CI) of the mean difference (bias) does not intersect zero then an adjustment should be made when converting from one measuring instrument to the other. The Assessment Group also extracted data on the regression between the index test and reference standard, but this can only give information on the correlation between the two measures, and is not informative to the question of whether the two measures can be considered equivalent. Significant correlation cannot be considered evidence for significant equivalence.

Quality Assessment Strategy

Adapting the Quality of Diagnostic Accuracy Studies (QUADAS-2) Checklist for Objective 1-A Data Extraction Strategy

Where appropriate, the quality of diagnostic accuracy studies was assessed using QUADAS-2. For reasons explained below QUADAS-2 was adapted for Objective A-1 (see Appendix 5 in the DAR).

QUADAS-2 is a broad tool to assess the quality of primary diagnostic accuracy studies. For this part of the review the Assessment Group was interested in analytic validity of the test only, i.e., its accuracy and reliability in measuring 5-fluorouracil (5-FU) plasma levels. Whether the test can accurately predict patients' response to and side effects of treatment (its clinical validity) and be implemented to improve patient outcomes (its clinical utility) are considered in Objectives B, C and D. Therefore the Assessment Group adapted the signalling questions in the QUADAS-2 tool for use with laboratory analytical studies. This was informed by the Analytic validity, Clinical validity, Clinical utility and Ethical (ACCE) guidance for assessing analytic validity for genetic tests.

See Section 4.1.5.1 in the DAR for more information.

Quality Assessment Strategy for Objectives B and C

For Objectives B and C, as a broad range of study designs were identified in the scoping searches, the use of a single checklist, in contrast to individual checklists for each study design, was considered appropriate. The Downs and Black (1998) checklist was therefore used to assess the quality of papers meeting the inclusion criteria (see Appendix 6 in the DAR). This 27-item checklist enabled an assessment of randomised and non-randomised studies and provides both an overall score for study quality and a profile of scores not only for the quality of reporting, internal validity (bias and confounding) and power, but also for external validity. However, since some questions were not appropriate for single arm studies, the overall score was not considered useful or appropriate and was therefore not used. The results of the quality assessment provide an overall description of the quality of the included studies and provide a transparent method of recommendation for design of any future studies. Quality assessment was undertaken by one reviewer and checked by a second reviewer, any disagreements were resolved by a third reviewer through discussion.

Methods of Analysis/Synthesis

Diagnostic Accuracy Studies (My5-FU versus HPLC/LC-MS) (Objective A-1)

The My5-FU assay delivers an estimate of plasma 5-FU concentration. For a study population this may potentially allow discrimination of study populations into categories: over-dosed, optimally-dosed and under-dosed. Where results from a gold standard were available, a 2x2 table was constructed allowing diagnostic accuracy to be estimated using standard statistics (e.g., sensitivity, specificity, positive and negative likelihood ratios, positive and negative predictive values).

Diagnostic accuracy studies (My5-FU versus HPLC/LC-MS) are considered to be those where patient samples are assayed for 5-FU concentration but patient outcomes may not be reported. Those studies that aimed to test the internal and/or external validity of the My5-FU assay were identified and their findings were summarised and appraised. Studies that do not report test failure rates were noted; where available, test failure rates were tabulated.

Patient-based Studies (Objectives B and C)

Analysis was stratified according to cancer type, 5-FU delivery mode and cancer stage (e.g., metastatic).

Study, treatment, population, and outcome characteristics were summarised and compared qualitatively and, where possible, quantitatively in text, graphically and in evidence tables. Pooling studies results by meta-analysis was considered. Where meta-analysis was considered unsuitable for some or all of the data identified (e.g., due to the heterogeneity and/or small numbers of studies), the Assessment Group employed a narrative synthesis. This involved the use of text and tables to summarise data allowing reader to consider any outcomes in the light of differences in study designs and potential sources of bias for each of the studies being reviewed. Studies were organised by research objective addressed. A commentary on the major methodological problems or biases that affected the studies was included, together with a description of how this may have affected the individual study results.

For Objectives B and C the Assessment Group aimed to identify studies which compared body surface area (BSA)-based dose regimens of 5-FU with continuous infusion in which measures of plasma 5-FU are not undertaken to inform dose changes with dose regimens in which dose adjustment is informed by the My5-FU assay results applied to a stated dose adjustment algorithm. These studies would best report the following outcomes: incidence and severity of side effects of 5-FU; overall survival and progression-free survival as stated in the inclusion criteria. The Assessment Group considered using a linked-evidence approach in which studies report dose adjustment informed by plasma 5-FU measured by other methods (e.g., HPLC, LC-MS); this required evidence of comparable performance of My5-FU with such assay methods.

See Section 4.1 in the DAR for more information about methods of analysis and synthesis.

Cost-effectiveness and Health Economics

Methods

Evaluation of Costs, Quality of Life and Cost-effectiveness

Model Structure

Where data allows, the preferred approach will be to model the impact of pharmacokinetic dose adjustment using My5-FU assay compared to BSA dosing, using specific clinical outcomes and with a lifetime horizon. In the absence of such evidence a linked evidence approach will be adopted, linking My5-FU dose adjustment to other pharmacokinetic dose adjustment studies within the literature. It may assume equivalence

between the My5-FU assay and other pharmacokinetic measures of plasma 5-FU (i.e., HPLC and LC-MS) if this appears a reasonable assumption in the light of the clinical review. Model inputs may utilise indirect treatment comparison results or network meta-analysis results to derive estimates of the clinical outcomes for the chemotherapy regimens relevant to current UK clinical practice. It is anticipated that this will be possible for metastatic colorectal cancer, as outlined in more detail in Section 5.2 in the DAR.

See Section 6 in the DAR for additional information on cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Developing Recommendations

After reviewing the evidence the Diagnostics Advisory Committee (DAC) agrees draft recommendations on the use of the technology in the National Health Service (NHS) in England. When formulating these recommendations, the Committee has discretion to consider those factors it believes are most appropriate to the evaluation. In doing so, the Committee has regard to any relevant provisions of the National Institute for Health and Care Excellence's (NICE's) Directions, set out by the Secretary of State for Health, and legislation on human rights, discrimination and equality. In undertaking evaluations of healthcare technologies, NICE takes into account the broad balance of clinical benefits and costs, the degree of clinical need of patients under consideration, any guidance issued to the NHS by the Secretary of State that is specifically drawn to the attention of NICE by the Secretary of State, and any guidance issued by the Secretary of State, and the potential for long-term benefits to the NHS of innovation.

The Committee takes into account advice from NICE on the approach it should take to making scientific and social value judgements. Advice on social value judgements is informed in part by the work of NICE's Citizens Council.

The Committee takes into account how its judgements have a bearing on distributive justice or legal requirements in relation to human rights, discrimination and equality. Such characteristics include, but are not confined to: race, gender, disability, religion or belief, sexual orientation, gender reassignment and pregnancy or maternity.

The Committee considers the application of other Board-approved NICE methods policies, such as the supplementary guidance on discounting and the end-of-life criteria, if they are relevant to the evaluation.

Because the Programme often evaluates new technologies that have a thin evidence base, in formulating its recommendations the Committee balances the quality and quantity of evidence with the expected value of the technology to the NHS and the public.

The credibility of the guidance produced by NICE depends on the transparency of the DAC's decision-making process. It is crucial that the DAC's decisions are explained clearly, and that the contributions of registered stakeholders and the views of members of the public are considered. The reasoning behind the Committee's recommendations is explained, with reference to the factors that have been taken into account.

The language and style used in the documents produced by the Committee are governed by the following principles:

- Clarity is essential in explaining how the DAC has come to its conclusions.
- The text of the documents does not need to reiterate all the factual information that can be found in the information published alongside the guidance. This needs careful judgement so that enough information and justification is given in the recommendations to enable the reader to understand what evidence the DAC considered and, if appropriate, who provided that evidence.

The Committee may take into account factors that may provide benefits to the NHS or the population, such as patient convenience. It may also consider costs and other positive or negative impacts on the NHS that may not be captured in the reference-case cost analysis, such as improved processes.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Two base-case analyses were developed:

- FOLFOX (oxaliplatin in combination with 5-flourouracil and folinic acid) base case: survival data drawn from a FOLFOX6 study supplemented with FOLFOX6 body surface area dosing studies
- 5-fluorouracil (5-FU) + folinic acid base case: survival data drawn from other studies supplemented with 5-FU + folinic acid body surface area dosing studies, combined with drug costs for FOLFOX6 (to represent UK practice)

A deterministic analysis of the FOLFOX6 base case produced an incremental cost-effectiveness ratio (ICER) of £4148 per quality-adjusted life year (QALY) gained for the My5-FU assay, based on an estimated gain of 0.599 QALYs and an incremental cost of £2483. A probabilistic sensitivity analysis based on 10,000 iterations was run, which also produced an ICER of £4148 per QALY gained for the My5-FU assay. At a maximum acceptable ICER of £20,000 per QALY gained, the probability that dose adjustment using the My5-FU assay is cost effective compared with body surface area dosing is 100%.

A deterministic analysis of the 5-FU + folinic acid base case produced an ICER of £5853 per QALY gained for the My5-FU assay. A probabilistic sensitivity analysis based on 10,000 iterations was run, which produced an ICER of £5852 per QALY gained for the My5-FU assay. At a maximum acceptable ICER of £20,000 per QALY gained, the probability that dose adjustment using the My5-FU assay is cost effective compared with body surface area dosing is 90%.

The Committee considered the results of the base-case sensitivity analyses and noted that the cost effectiveness of the My5-FU assay was dependent on increased overall survival being realised in practice, because the reduction in toxicities alone was not sufficient to offset the increased costs associated with the My5-FU assay in the economic model. When the relative progression-free and overall survival effect estimates were removed from the economic model, the resulting ICERs were £435,819 per QALY gained in the FOLFOX6 analysis and £435,804 per QALY gained in the 5-FU + folinic acid analysis. The Committee therefore concluded that the uncertainty associated with the reported ICERs was too great to conclude that the use of the My5-FU assay would be cost effective in routine clinical practice.

The Committee considered that the most notable benefit associated with pharmacokinetic dose adjustment of continuous infusion 5-FU was its potential to increase the number of people having optimal therapeutic doses without increasing toxicities, but concluded that further research was needed to confirm whether this would be achieved in practice.

The Committee acknowledged that many clinicians now prescribe capecitabine as an alternative to 5-FU and noted that the My5-FU assay is not licensed for use with capecitabine. The Committee heard from clinical specialists that around 30% to 40% of colorectal cancer patients currently receive continuous infusion 5-FU and that recently licensed biological agents are marketed for use in conjunction with continuous infusion 5-FU. The Committee concluded that it was likely that there will continue to be a significant proportion of patients who receive continuous infusion 5-FU, and who may benefit from pharmacokinetic dose adjustment in the future.

See Sections 5 and 6 in the original guideline document for more information on cost-effectiveness.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

The National Institute for Health and Care Excellence (NICE) sends the Diagnostics Assessment Report (DAR), with any confidential material removed, to registered stakeholders for comment. Stakeholders have 10 working days to return comments. Models supporting the DAR are made available to registered stakeholders on request during this period.

NICE presents anonymised registered stakeholder comments on the DAR, along with any responses from NICE or the External Assessment Group (EAG), to the Committee and later publishes these comments on its website.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Diagnostics Advisory Committee considered clinical and cost-effectiveness of the My5-FU assay from a Diagnostics Assessment Report prepared by an External Assessment Group.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Pharmacokinetic dose adjustment of 5-fluorouracil (5-FU) may result in increased overall and progression-free survival, by increasing the number of people having an optimum therapeutic dose of 5-FU and by reducing the incidence of side effects and toxicities.

Potential Harms

Side effects from laboratory and pathology tests are usually limited to the side effects resulting from obtaining the sample. However, in some cases, dietary or other changes are required of the patient before the test.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Care Excellence (NICE) and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Care Excellence (NICE) will support this guidance through a range of activities to promote the recommendations for further research. The research proposed will be passed to the NICE Medical Technologies Evaluation Programme research facilitation team for the development of specific research trial protocols as appropriate. NICE will also incorporate the research recommendations in section 7 of the original guideline document into its guidance research recommendations database (available on the NICE website) and highlight these recommendations to public research bodies.

Implementation Tools

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Fluorouracil chemotherapy: the My5-FU assay for guiding dose adjustment. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Dec 10. 47 p. (Diagnostics guidance; no. 16).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2014 Dec 10

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Diagnostics Advisory Committee

Composition of Group That Authored the Guideline

Standing Committee Members: Professor Adrian Newland (*Chair, Diagnostics Advisory Committee*); Dr Mark Kroese (*Vice Chair, Diagnostics Advisory Committee*), Consultant in Public Health Medicine, PHG Foundation, Cambridge and UK Genetic Testing Network; Professor Ron Akehurst, Professor in Health Economics, School of Health and Related Research (ScHARR), University of Sheffield; Professor Paul Collinson, Consultant Chemical Pathologist & Professor of Cardiovascular Biomarkers, St George's Hospital; Dr Sue Crawford, General Practitioner (GP) Principal, Chillington Health Centre; Professor Ian A Cree, Senior Clinical Advisor, NIHR Evaluation Trials and Studies Coordinating Centre, University of Southampton; Professor Erika Denton, National Clinical Director for Diagnostics, NHS England, Honorary Professor of Radiology, University of East Anglia and Norfolk and Norwich University Hospital; Dr Steve Edwards, Head of Health Technology Assessment, BMJ Evidence Centre; Mr David Evans, Lay member; Dr Simon Fleming, Consultant in Clinical Biochemistry and Metabolic Medicine, Royal Cornwall Hospital; Mr John Hitchman, Lay Member; Professor Chris Hyde, Professor of Public Health and Clinical Epidemiology, Peninsula Technology Assessment Group (PenTAG); Mr Matthew Lowry, Director of Finance and Infrastructure, Doncaster and Bassetlaw Hospitals NHS Foundation Trust; Dr Michael Messenger, Deputy Director and Scientific Manager NIHR Diagnostic Evidence Co-operative, Leeds; Dr Peter Naylor, General Practitioner (GP), Chair Wirral Health Commissioning Consortia; Dr Dermot Neely, Consultant in Clinical Biochemistry and Metabolic Medicine, Newcastle upon Tyne NHS Trust; Dr Richard Nicholas, Consultant Neurologist, Honorary Senior Lecturer, Heatherwood and Wexham Park Hospitals; Dr Gail Norbury, Consultant Clinical Scientist, Guys Hospital; Dr Diego Ossa, Director of Market Access Europe, Novartis Molecular Diagnostics; Professor Mark Sculpher, Professor of Health Economics, Centre for Health Economics, University of York; Dr Steve Thomas, Consultant Vascular and Cardiac Radiologist, Sheffield Teaching Hospitals Foundation Trust; Mr Paul Weinberger, CEO, DiaSolve Ltd, London

Specialist Committee Members: Dr Nick Wadd, Consultant Clinical Oncologist, South Tees Hospitals NHS Foundation Trust; Dr Gireesh Kumaran, Consultant Medical Oncologist, The Mid Yorkshire Hospitals NHS Trust; Joanne Lowe, Clinical Pharmacist (Gastrointestinal/Palliative Care), The Christie NHS Foundation Trust; Ann Cole, Lay member; Anne-Marie Hunter, Lay member

Financial Disclosures/Conflicts of Interest

Committee members are required to submit a declaration of interests on appointment, in every year of their tenure, and at each Committee meeting, in line with the National Institute for Health and Care Excellence's (NICE's) code of practice for declaring and dealing with conflicts of interest.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download as a Kindle or EPUB ebook from the NICE Web site .

Availability of Companion Documents

The following are available:

- Fluorouracil chemotherapy: the My5â€‘FU assay for guiding dose adjustment. Costing statement. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Dec. 1 p. (Diagnostics guidance; no. 16). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Freeman K, Connock M, Cummins E, Gurung T, Taylor-Phillips S, Court R, Saunders M, Clarke A, Sutcliffe P. Fluorouracil plasma monitoring: the My5-FU assay for guiding dose adjustment in patients receiving fluorouracil chemotherapy by continuous infusion. Diagnostics Assessment Report commissioned by the NIHR HTA Programme on behalf of the National Institute for Health and Care Excellence. Warwick (UK): Warwick Evidence Group; 2014 Jun. 401 p. Electronic copies; Available from the NICE Web site .

- Diagnostics Assessment Programme manual. London (UK): National Institute for Health and Care Excellence; 2011 Dec. 130 p. Electronic copies: Available from the NICE Web site .

Patient Resources

The following is available:

- Fluorouracil chemotherapy: the My5â€‘FU assay for guiding dose adjustment. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Dec. (Diagnostics guidance; no. 16). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on February 18, 2015.

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